Ancylostoma braziliense, Ancylostoma caninum, Ancylostoma ceylanicum, Ancylostoma. tubaeforme, Bunostomum phlebotomum, Uncinaria stenocephala,

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Importance

Hookworms are parasitic intestinal nematodes, several of which are zoonotic. In their normal hosts, hookworms may enter the body either by ingestion or through the skin. Larvae that penetrate the skin travel through various organs, including the respiratory tract, before entering the intestines and developing into mature hookworms. Hookworms can cause anemia, abdominal pain and diarrhea when they reside in the intestines, or respiratory, dermatologic and other signs during their migration through the body. Young individuals tend to be affected more severely. In cattle, infections may lead to severe disease and pronounced weight loss, with as few as 50 adult worms causing significant anemia in calves. Hookworm disease in cats and dogs can result in anemia, and infections of neonatal pups may prove fatal, even with as few as 50-100 worms present.

Animal hookworm larvae can penetrate the human epidermis, but most species cannot readily enter the dermis, and remain trapped in the skin. These larvae migrate extensively within the skin for a time, resulting in a highly pruritic but self-limited disease called cutaneous larva migrans. One species carried by dogs and cats is increasingly recognized as an intestinal parasite of humans: *Ancylostoma ceylanicum* has been found in 6-23% of patent human hookworm infections in some parts of Asia. *A. caninum* also migrates occasionally to the intestines, but usually as a single worm. While one hookworm is unlikely to cause significant blood loss, its presence may result in a painful intestinal disorder called eosinophilic enteritis.

Etiology

Hookworms are nematodes in the superfamily Ancylostomatoidea. In their normal hosts, they are parasites of the intestinal tract. Humans are usually infected by *Ancylostoma duodenale* and *Necator americanus*, which are maintained in human populations. Some zoonotic species may also reach the intestines. *A. ceylanicum* can sometimes be found in large enough numbers to cause typical enteric signs, but *A. caninum* seems to occur only as a single worm. Rare human intestinal infections with *A. malayanum*, *A. japonica*, *Necator suillis* and *N. argentinus* have also been reported, but the identification of these organisms is uncertain.

Hookworm larvae that normally mature in the intestinal tracts of animals can cause cutaneous larva migrans in people. Zoonotic hookworms known to cause this condition include *A. braziliense*, *A. caninum*, *A. ceylanicum*, *A. tubaeforme*, *Uncinaria stenocephala* and *Bunostomum phlebotomum*. Other species of hookworms found in animals, including wildlife and captive exotics, might also be able to cause cutaneous larva migrans.

Species Affected

Ancylostoma braziliense is a hookworm of dogs, cats and other carnivores. A. caninum is found in dogs, and has been reported in cats in some parts of Asia and Australia. Uncinaria stenocephala also infects dogs and occasionally cats. A. ceylanicum occurs in wild and domesticated canids and felids, and A. tubaeforme infects cats and other felids. Bunostomum phlebotomum is a hookworm of cattle. Rodents can be paratenic hosts for hookworms including A. braziliense, A. tubaeforme, and U. stenocephala, and possibly other hookworm species.

Ancylostoma duodenale and Necator americanus, species usually found only in humans, have been reported on rare occasions in other mammals.

Zoonotic potential

A. braziliense is responsible for most cases of cutaneous larva migrans in humans. A. caninum, A. ceylanicum, Uncinaria stenocephala and Bunostomum phlebotomum are involved less frequently, while rare cases have been caused by A. tubaeforme.

A. ceylanicum is the only zoonotic hookworm known to produce patent intestinal infections in humans. A. caninum can cause eosinophilic enteritis, but does not seem to become patent.

Geographic Distribution

A. caninum is the most widespread of all hookworms and can be found in many parts of the world. A. tubaeforme is also widely distributed. A. braziliense is limited to tropical and subtropical regions including Central and South America, the Caribbean and parts of the U.S. A ceylanicum has been reported in parts of Asia, Africa, Australia, and the Middle East, and in one publication from Brazil. B. phlebotomum is a parasite of temperate regions, while U. stenocephala occurs in colder climates including Canada, the northern U.S. and Europe.

Transmission and Life Cycle

Adult hookworms live in the intestines. Hookworm eggs shed in the feces are not immediately infective, and hatch in the environment, often within one to a few days. The larvae feed on soil bacteria and molt twice before they become infective third stage larvae. The larvae develop best in warm, moist, sandy soil that is sheltered from direct sunlight. Under optimal conditions, they reach the infective stage in approximately 4 to 7 days. Third-stage larvae that are unable to enter a mammalian host die in approximately 1 to 2 months when their metabolic reserves are exhausted.

Larvae may enter the body either by penetrating the skin, or by ingestion. Penetration of the skin by third stage larvae usually requires at least 5 to 10 minutes contact with contaminated soil. In their natural hosts, these larvae enter the dermis, where they are transported through the lymphatic vessels and veins to the lungs. In the lungs, they penetrate the alveoli and migrate up the respiratory tree to the trachea. They are swallowed and mature into adults in the intestines. Ingested hookworm larvae do not follow this route, but they develop for a period of time in the gastrointestinal wall before re-appearing in the lumen and maturing to adult worms. A. caninum, A. braziliense, A. ceylanicum and B. phlebotomum can either penetrate the skin or be ingested. U. stenocephala is usually acquired by ingestion.

In dogs more than three months old, *A. caninum* larvae may fail to complete the migration through the lungs and are arrested in the tissues, where they survive as dormant (hypobiotic) larvae. These larvae can move to the uterus or mammary gland during pregnancy, and are transmitted to the pups. This route of transmission does not seem to exist for *A. braziliense* or *U. stenocephala* in dogs, or for any hookworms in cats or cattle.

In the intestines, adult hookworms are attached to the mucosa, but change their location every few hours, leaving tiny, bleeding mucosal ulcerations behind. Some species such as *A. caninum* release a strong anticoagulant that can cause profuse bleeding. Adult hookworms can live for months to a year or more. Reported adult lifespans are approximately 4 to 8 months for *A. braziliense*, 18 months to 2 years for *A. tubaeforme*, and about 4 months to a year for *U. stenocephala* in dogs. The prepatent period varies with the species of parasite, host species and route of exposure. Canine and feline hookworms usually become patent after

13-27 days; however, *A. caninum* infections transmitted in colostrum or *in utero* can produce eggs during the second week of life. The prepatent period for *B. phlebotomum* in cattle is approximately two months. Eggs may be shed intermittently.

Infections in paratenic hosts

Paratenic (transport) hosts can be infected orally or through the skin. Larvae do not develop further in paratenic hosts, but become dormant in various tissues. In mice, *A. braziliense* and *A. tubaeforme* larvae are mainly found in the head, particularly in the nasopharyngeal epithelium and salivary glands. *A. caninum* and *U. stenocephala* occur mainly in the muscles. If a definitive host ingests these larvae, they are released and complete their development to adults.

Infections in humans

In humans, most zoonotic hookworm larvae cannot penetrate into the dermis. They remain confined to the epidermis, where they migrate for a period of time but eventually die. These organisms cannot be transmitted to others.

A. caninum can occasionally be found in human intestines, while A. ceylanicum seems to occur more frequently. The route of infection with A. caninum is still unknown; either percutaneous or oral transmission may be possible. Infections with this organism do not seem to become patent; only single A. caninum worms have ever been found in humans. A. ceylanicum, however, can mature, mate and produce eggs in people. Patients with intestinal hookworm disease (A. ceylanicum) are not directly contagious to others, as the eggs must develop for a period of time in the soil before they develop into infective third stage larvae. However, the eggs they shed can contaminate the soil. Epidemiological and genetic data suggest that A. ceylanicum may cycle between humans, dogs and cats in some hookworm-endemic communities in Southeast Asia. It is possible that this occurs in other locations as well.

Disinfection

Aqueous iodine at 50-60 parts per million at 15-30°C (59-86 °F) has been reported to kill hookworm larvae in 15 minutes or less. Other agents which were shown to kill larvae of *Necator americanus* in a laboratory setting include very hot water (above 80°C, 176°F), ethanol (70% for 10 minutes contact time), and Dettol® (0.5% for 15 minutes contact time). In the same study, sodium hypochlorite (bleach, 1%) and glutaraldehyde (2%) had no killing effect on *N. americanus* larvae, and the efficacy of these agents on the larvae of other hookworm species is questionable. Sodium borate (1kg/2 m²) can be used to disinfect the soil. Hookworm larvae are also susceptible to freezing, drying, direct sunlight and temperatures above 45°C (113°F).

Infections in Animals

Incubation Period

The incubation period varies with the number of parasites. Puppies can become symptomatic in the first week of life, before the infection becomes patent.

Clinical Signs

Dogs and cats

The clinical signs caused by adult hookworms vary with the parasite burden and the age of the animal. They are frequently related to enteritis and/or intestinal blood loss, and are generally more severe in young animals.

In dogs, *A. caninum* can cause anemia, dark reddishbrown to black hemorrhagic diarrhea, anorexia and dehydration, with associated weakness. Death may occur due to blood loss. The worms can also cause protein and fluid loss and malabsorption, resulting in wasting and decreased growth. Older animals can carry a few worms without clinical signs. Similarly, *A. tubaeforme* can cause intestinal blood loss, anemia and weight loss in kittens, and large numbers of worms can be fatal. In contrast, *U. stenocephala* and *A. braziliense* are not heavy blood-feeders and do not cause anemia or bloody diarrhea. However, they can result in enteric disease, including diarrhea and protein-losing enteropathy.

Larval hookworms may also cause clinical signs during their migration. Dermatitis may be seen where they penetrate the skin. The cutaneous lesions, which can include erythema, pruritus and papules, are usually limited to the feet and often to the interdigital spaces. In some cases, these signs may be severe and result in self-inflicted trauma. Most often, the skin lesions disappear approximately five days after they appear. Large numbers of larvae in puppies can cause pneumonia during their migration through the lungs. Rarely, aberrant larvae in other locations (e.g., the spinal cord) may also become symptomatic.

Cattle

Larval penetration of the lower limbs can cause uneasiness and stamping, and there may be local skin lesions, edema and scabs. The adult worms can cause anemia, rapid weight loss, and alternating diarrhea and constipation. Hypoproteinemia may be seen, but bottle jaw is usually mild. Deaths can occur, especially in calves.

Post Mortem Lesions di Click to view images

Hookworms are small, grayish-white to reddish-white, cylindrical nematodes (approximately 5-20 mm long), found in the intestines. The intestinal mucosa may be congested and swollen, with many tiny hemorrhagic points or ulcers. With many hookworm species, the intestinal contents are bloodstained. In animals with anemia, the liver and other organs may appear pale.

Pneumonia and lung consolidation can be seen with large numbers of larvae in puppies. Skin lesions may be

found on the feet, particularly between the toes where the larvae penetrated. Larvae in aberrant sites may be associated with necrotic and hemorrhagic tracts in the tissues, as well as other signs of tissue damage.

Diagnostic Tests

Hookworm infections are diagnosed by fecal flotation and detection of the eggs. Typical Ancylostoma eggs are 55 -76 μm in length and approximately 34-50 μm in width, and have a smooth, thin outer shell. They are unembryonated when they are first shed, but develop quickly; at the time of diagnosis, they may contain several cells or a ball of cells. Uncinaria spp. eggs are very similar but slightly larger (70 -90 μm x 40-50 μm); they cannot be easily distinguished from Ancylostoma spp. except in mixed infections. First-stage hookworm larvae may appear in preparations from old or stored feces, especially in warm and humid conditions. Eggs are not shed constantly, and repeated sampling may be necessary to detect infections. Coproantigen ELISA tests are in development.

Hookworm larvae can be identified by fecal culture, if identification to the species level is important. Adult worms can be differentiated by their morphology, using published keys. Polymerase chain reaction (PCR) assays have been used in research.

Treatment

Hookworms can be treated with a wide variety of anthelmintics, however, resistance has been detected in the case of some commonly used drugs such as pyrantel in dogs. Supportive care such as supplemental iron, blood transfusions or a high protein diet may also be necessary in some cases.

Prevention

Anthelmintics can be used in ruminants to decrease parasite burdens and pasture contamination. Pasture rotation and other management techniques can also be important components in preventing disease.

Some heartworm preventives may also aid in the prevention of hookworm disease in dogs and cats. Concrete runways, washed at least twice a week in warm weather, should be used for dogs housed in kennels. Clay or sandy runways, as well as soil and lawns, can be decontaminated with sodium borate. To prevent *A. caninum* infections in puppies, bitches should be free of hookworms, and they should be kept out of contaminated areas during their pregnancy. The dam and puppies should also be housed separately from other animals.

Infections in cats can be decreased by keeping cats indoors and preventing them from eating rodents. Keeping the litter box clean may decrease reinfection.

Morbidity and Mortality

Hookworms are common parasites of cats and dogs. Although their prevalence can vary, species such as *A. caninum* or *A. tubaeforme* may infect most of the dogs and

cats in some tropical regions. *A. ceylanicum* is also common in some communities in Asia. In one study, *A. ceylanicum* was found in 46% of hookworm-infected dogs and cats in a rural community in Malaysia, where nearly 25% of hookworm-positive humans were found to be infected with this same species.

A. caninum and A. tubaeforme infections are generally more serious than U. stenocephala and A. braziliense. Some A. caninum and A. tubaeforme infections may be fatal, particularly in young animals, due to blood loss. B. phlebotomum can cause deaths in calves.

Infections in Humans

Incubation Period

The incubation period for cutaneous larva migrans is short but vaguely established; according to some estimates, it is approximately 1 to 2 weeks. The incubation period for intestinal hookworm disease varies with the number of parasites and can be a few weeks to many months.

Clinical Signs

Cutaneous larva migrans

Cutaneous larva migrans is the most common syndrome caused by zoonotic hookworms in humans. Most lesions occur on the legs, buttocks and hands, but they can be found on any part of the body that was exposed to the soil. Initially, there may be a tingling or prickling sensation where the larvae penetrated the skin, followed by a papule at the same location.

Migration of the slow-moving larvae in the skin results in an allergic reaction where they tunnel. The lesions may include papules as well as nonspecific dermatitis, vesicles, or narrow, serpiginous (snakelike), slightly elevated, erythematous lines. The lesions are intensely pruritic, especially at night, and usually advance several millimeters to a few centimeters a day. Pain is occasionally reported, usually in association with vesicles. Secondary bacterial infections can occur due to scratching. Most cases resolve spontaneously in a few days to several weeks, but some untreated lesions have been reported to last for more than a year.

Other lesions are occasionally reported, when larvae penetrate beyond the epidermis. *A. caninum* larvae may migrate to the muscles, resulting in myositis with persistent swelling and tenderness. These larvae can also cause systemic signs and folliculitis. *Ancylostoma* spp. larvae have been documented in the eye.

Classic (intestinal) hookworm disease

Although intestinal hookworm disease is usually caused by human hookworms, the zoonotic species *A. ceylanicum* can also cause this syndrome. With hookworms adapted to humans, the first symptom is usually pruritus at the site of larval penetration. There may also be erythema with small papules or vesicles, which usually persists for 1 to 2 weeks.

Migration of the larvae through the lungs may cause coughing and wheezing; however, lung signs are uncommon and are usually mild except with very heavy worm burdens. The adult worms can cause acute intestinal signs such as abdominal pain, nausea, anorexia, vomiting and hemorrhagic diarrhea or melena. Chronic hookworm disease is characterized by blood loss and iron-deficiency anemia, and is associated with fatigue, pallor, tachycardia and dyspnea on exertion. Hypoproteinemia may cause edema, and there can be signs of malabsorption and malnutrition. In children, there may also be adverse effects on physical and intellectual growth. The severity of the disease varies with the worm burden and the amount of blood loss. Heavy infections can be fatal, particularly in infants.

A. ceylanicum infections tend to be milder than those caused by human hookworms. Anemia is usually the most prominent symptom, but other clinical signs, similar to those caused by the human hookworms, are also reported.

Eosinophilic enteritis

Eosinophilic enteritis is caused by the zoonotic hookworm *A. caninum*. It is characterized by increasingly severe episodes of abdominal pain associated with peripheral eosinophilia, but no blood loss. Severe cases can mimic appendicitis or intestinal perforation. Some *A. caninum* infections may be asymptomatic.

Diagnostic Tests

Cutaneous Iarva migrans

A presumptive diagnosis of cutaneous larva migrans is usually made based on the clinical signs. It may be possible to confirm the diagnosis by a biopsy of the affected skin; however, the larvae are rarely found and this test is not usually diagnostic.

Classic (intestinal) hookworm disease

Intestinal hookworm infections, including *A. ceylanicum*, are diagnosed by identifying the eggs in the feces, as for animals.

Eosinophilic enteritis

A. caninum infections are difficult to diagnose. The parasite cannot be detected by examination of the feces, as the single worms found in human hosts do not produce eggs. The presence of eosinophilia aids in diagnosis. Ulcerations in the ileum and colon, and occasionally hookworms, may be seen during colonoscopy. Serologic tests for hookworms, including ELISAs and immunoblotting (Western blotting) are used only in research.

Treatment

Intestinal disease

Hookworms in the intestines can be treated with a variety of anthelmintics. Iron therapy or blood transfusions may also be needed. In hookworm endemic regions, reinfection is likely, in that currently utilized anti-nematode drugs do not confer lasting protection.

Cutaneous larva migrans

Cutaneous larva migrans can be treated with topical or oral anthelmintics. Patients with minimal symptoms may not require treatment, as the infection is self-limiting. Pruritus usually decreases within 24 to 48 hours after the initial treatment, and the lesions usually resolve in a week.

Prevention

Zoonotic hookworm disease is best prevented by eliminating the parasites from dogs and cats to decrease contamination of the soil. Dogs and cats should also be kept off beaches and other places where children play in the sand. Sandboxes should be covered when not in use. Sodium borate can be used to sterilize lawns, kennels or other areas. Removing canine feces at least twice a week also decreases soil contamination. The larvae do not survive well in dry, bare soil in direct sunlight.

Prolonged skin contact with contaminated soil should be avoided. Wearing footwear (or gloves when gardening) can decrease the risk of infection. A waterproof sheet may be spread over damp work areas, when working under houses or in other potentially contaminated areas. When visiting the beach, wearing protective footwear, and using waterproof groundcovers rather than towels for sunbathing can help prevent contact with potentially contaminated sand.

Hookworms can be acquired by ingestion as well as skin contact; therefore, unsafe water should be boiled, and potentially contaminated foods avoided. The hands should also be washed before eating and after contact with soil or other sources of hookworms.

Morbidity and Mortality

Cutaneous larva migrans is particularly common in children. The prevalence is also high in adults who have close contact with soil or sand, including gardeners, farmers, miners, exterminators and others whose occupations require crawling under houses. Cutaneous larva migrans is the most common travel-related skin infection in tourists to tropical areas. Infections are self-limiting and the lesions resolve within a few weeks to a few months. Rare cases have lasted up to a year. Deaths are not seen.

Intestinal infections with *A. caninum* seem to be uncommon. Human intestinal infections with *A. ceylanicum* are common in some parts of Asia, and possibly other regions. Classic intestinal hookworm disease caused by human hookworms can result in anemia, malnutrition, and, in severe cases, congestive heart failure, severe blood loss or death, especially in young children. The potential for zoonotic intestinal hookworms (*A. ceylanicum*) to cause severe disease (including non-blood loss related cognitive impairment) or death following natural infection needs further study.

Internet Resources

Centers for Disease Control and Prevention (CDC)

CDC Guidelines for Veterinarians: Prevention of Zoonotic Transmission of Ascarids and Hookworms of Dogs and Cats

<u>Public Health Agency of Canada. Pathogen Safety Data Sheets.</u>

The Merck Manual

The Merck Veterinary Manual

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